

Case No. 21036YP  
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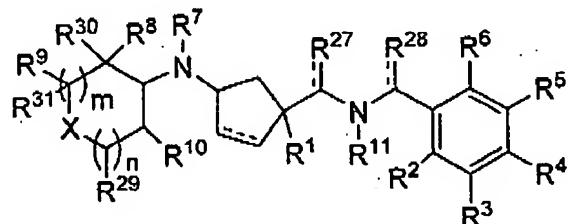
OCT 05 2007

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (currently amended) A compound of the formula I:



I

wherein:

X is selected from the group consisting of:

-O-, -NR<sup>20</sup>-, -S-, -SO-, -SO<sub>2</sub>-, and -CR<sup>21</sup>R<sup>22</sup>-, -NSO<sub>2</sub>R<sup>20</sup>-,

-NCOR<sup>20</sup>-, -NCO<sub>2</sub>R<sup>20</sup>-, -CR<sup>21</sup>CO<sub>2</sub>R<sup>20</sup>-, -CR<sup>21</sup>OCOR<sup>20</sup>-, -CO-, -O-C(CH<sub>3</sub>)<sub>2</sub>-O-,

where R<sup>20</sup> is selected from: hydrogen, C1-6 alkyl, benzyl, phenyl,

C<sub>3</sub>-6 cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, C<sub>1</sub>-3alkyl, C<sub>1</sub>-3alkoxy, -CO<sub>2</sub>H, -CO<sub>2</sub>-C<sub>1</sub>-6 alkyl, and trifluoromethyl,

where R<sup>21</sup> and R<sup>22</sup> are independently selected from: hydrogen, hydroxy,

C<sub>1</sub>-6 alkyl, -O-C<sub>1</sub>-6alkyl, benzyl, phenyl, C<sub>3</sub>-6 cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, C<sub>1</sub>-3alkyl, C<sub>1</sub>-3alkoxy, -CO<sub>2</sub>H, -CO<sub>2</sub>-C<sub>1</sub>-6 alkyl, and trifluoromethyl;

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$R^1$  is selected from:

-C<sub>1-6</sub>alkyl, -C<sub>0-6</sub>alkyl-O-C<sub>1-6</sub>alkyl, -C<sub>0-6</sub>alkyl-S-C<sub>1-6</sub>alkyl,  
-C<sub>0-6</sub>alkyl-SO<sub>1-2</sub>-C<sub>1-6</sub>alkyl, -C<sub>0-6</sub>alkyl-SO<sub>2</sub>-NR<sup>26</sup>-C<sub>1-6</sub>alkyl, -(C<sub>0-6</sub>alkyl)-  
(C<sub>3-7</sub>cycloalkyl)-(C<sub>0-6</sub>alkyl), hydroxy, -CO<sub>2</sub>R<sup>20</sup>, heterocycle, -CN, -  
NR<sup>20</sup>R<sup>26</sup>, -NR<sup>26</sup>SO<sub>2</sub>R<sup>20</sup>, -NR<sup>26</sup>COR<sup>21</sup>, -OCOR<sup>20</sup>, and phenyl,

where  $R^{26}$  is selected from: hydrogen, C<sub>1-6</sub> alkyl, benzyl, phenyl, C<sub>3-6</sub> cycloalkyl  
where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or  
substituted with 1-3 substituents where the substituents are independently  
selected from: halo, hydroxy, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, -CO<sub>2</sub>H, -CO<sub>2</sub>-C<sub>1-6</sub>  
alkyl, and trifluoromethyl trifluoromethyl,

where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7  
substituents where the substituents are independently selected from: halo,  
hydroxy, -O-C<sub>1-3</sub>alkyl, trifluoromethyl, C<sub>1-3</sub>alkyl, -O-C<sub>1-3</sub>alkyl, -CO<sub>2</sub>R<sup>20</sup>, -  
SO<sub>2</sub>R<sup>20</sup>, -NHCOC<sub>3</sub>, -NHSO<sub>2</sub>CH<sub>3</sub>, -heterocycle, =O, and -CN,

and where the phenyl and heterocycle are unsubstituted or substituted with 1-3  
substituents where the substituents are independently selected from: halo, hydroxy,  
C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy and trifluoromethyl;

$R^2$  is selected from: hydrogen, C<sub>1-6</sub>alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo,  
and phenyl;

$R^3$  is selected from: hydrogen, hydroxy, halo, C<sub>1-6</sub>alkyl, -O-C<sub>1-6</sub>alkyl, -NR<sup>20</sup>R<sup>21</sup>,  
-NR<sup>20</sup>CO<sub>2</sub>R<sup>21</sup>, -NR<sup>20</sup>CONR<sup>20</sup>R<sup>21</sup>, -NR<sup>20</sup>-SO<sub>2</sub>-NR<sup>20</sup>R<sup>21</sup>,  
-NR<sup>20</sup>-SO<sub>2</sub>-R<sup>21</sup>, heterocycle, -CN, -CONR<sup>20</sup>R<sup>21</sup>, -CO<sub>2</sub>R<sup>20</sup>, -NO<sub>2</sub>, -  
S-R<sup>20</sup>, -SO-R<sup>20</sup>, -SO<sub>2</sub>-R<sup>20</sup>, and -SO<sub>2</sub>-NR<sup>20</sup>R<sup>21</sup>;

R<sup>4</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

R<sup>5</sup> is selected from: C<sub>1</sub>-6alkyl substituted with 1-6 fluoro and optionally substituted with hydroxyl, -O-C<sub>1</sub>-6alkyl substituted with 1-6 fluoro, -CO-C<sub>1</sub>-6alkyl substituted with 1-6 fluoro, -S-C<sub>1</sub>-6alkyl, -pyridyl, fluoro, chloro, bromo, and phenyl;

R<sup>6</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

R<sup>7</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, and trifluoromethyl;

R<sup>8</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C<sub>1</sub>-3alkoxy, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, fluoro, -O-C<sub>1</sub>-3alkyl, where alkyl may be unsubstituted or substituted with 1-3 fluoro, and C<sub>3</sub>-6 cycloalkyl, -O-C<sub>3</sub>-6cycloalkyl, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, -OCOR<sup>20</sup>, and phenyl,

or R<sup>7</sup> and R<sup>8</sup> may be joined together via a C<sub>2</sub>-4alkyl or a C<sub>0</sub>-2alkyl-O-C<sub>1</sub>-3alkyl chain to form a 5-7 membered ring;

R<sup>9</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C<sub>1</sub>-3alkoxy, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, CO<sub>2</sub>R<sup>20</sup>, hydroxy, and -O-C<sub>1</sub>-6alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C<sub>1</sub>-3alkoxy, hydroxy, and -CO<sub>2</sub>R<sup>20</sup>,

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or R<sup>8</sup> and R<sup>9</sup> may be joined together by a C<sub>1</sub>-4alkyl chain or a C<sub>0-3</sub>alkyl-O-C<sub>0-3</sub>alkyl chain to form a 3-6 membered ring;

R<sup>10</sup> is selected from: hydrogen, and C<sub>1-6</sub>alkyl, where alkyl may be unsubstituted or substituted with 1-6 fluoro, fluoro, -O-C<sub>3-6</sub>cycloalkyl, and -O-C<sub>1-3</sub>alkyl, where alkyl may be unsubstituted or substituted with 1-6 fluoro,

or R<sup>8</sup> and R<sup>10</sup> may be joined together by a C<sub>1-3</sub>alkyl chain or a single bond to form a 3-6 membered ring; where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy,

or R<sup>8</sup> and R<sup>10</sup> may be joined together by a C<sub>1-2</sub>alkyl-O-C<sub>1-2</sub>alkyl chain to form a 6-8 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy,

or R<sup>8</sup> and R<sup>10</sup> may be joined together by a -O-C<sub>1-2</sub>alkyl-O- chain to form a 6-7 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy;

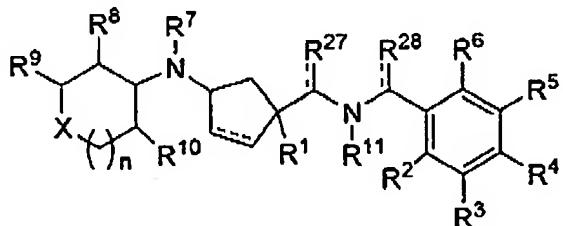
R<sup>11</sup> is selected from: hydrogen, C<sub>1-6</sub>alkyl, and trifluoromethyl;

R<sup>27</sup> and R<sup>28</sup> are independently selected from: =O, where R<sup>27</sup>, R<sup>28</sup>, or both, is oxygen and is connected via a double bond, hydrogen, phenyl, and C<sub>1-6</sub>alkyl which may be substituted or unsubstituted with 1-6 of the following substituents:

-COR<sup>11</sup>, hydroxy, fluoro, chloro, and -O-C<sub>1-3</sub>alkyl;

R<sup>29</sup>, R<sup>30</sup>, and R<sup>31</sup> are independently selected from: hydrogen, methyl, hydroxyl, trifluoromethyl, methoxy, and trifluoromethoxy;  
 or R<sup>29</sup> and R<sup>9</sup> are connected by a C<sub>1</sub>-salkyl bridge;  
 m is selected from 0, 1, and 2;  
 n is selected from 0, 1 and 2; and  
 the dashed line represents a single or a double bond;  
 and or a pharmaceutically acceptable salts salt thereof, and individual diastereomers thereof.

2. (currently amended) The compound of Claim 1 of the formula Ia:



1a

and or a pharmaceutically acceptable salt salts and individual diastereomers thereof.

3. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of: -O-, and -CH<sub>2</sub>-.

4. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein X is -O-.

5. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>1</sup> is selected from:

(1) -C<sub>1</sub>-6alkyl, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, hydroxy, -O-C<sub>1</sub>-3alkyl, and trifluoromethyl,

- (2) -C<sub>0</sub>-6alkyl-O-C<sub>1</sub>-6alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, and trifluoromethyl,
- (3) -C<sub>0</sub>-6alkyl-S-C<sub>1</sub>-6alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, and trifluoromethyl, and
- (4) -(C<sub>3</sub>-5cycloalkyl)-(C<sub>0</sub>-6alkyl), which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from: halo, hydroxy, -O-C<sub>1</sub>-3alkyl, and trifluoromethyl.

6. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>1</sup> is C<sub>1</sub>-6alkyl which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: hydroxy, and fluoro.

7. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:  
R<sup>1</sup> is selected from: isopropyl, -CH(OH)CH<sub>3</sub>, and -CH<sub>2</sub>CF<sub>3</sub>.

8. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:  
R<sup>2</sup> is selected from: hydrogen, hydroxy, and trifluoromethyl.

9. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:  
R<sup>2</sup> is selected from: hydrogen, and hydroxy.

10. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

$R^3$  is selected from:  $C_1$ -alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro, fluore, chloro, and bromo.

11. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

In the present invention it is more preferred that  $R^3$  is selected from: trifluoromethyl, trifluoromethyl, cyclopropyl, and fluoro.

12. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

$R^5$  is selected from:  $C_1$ -alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluore, fluoro, chloro, and bromo.

13. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

$R^5$  is selected from: trifluoromethyl, trifluoromethyl, cyclopropyl, and fluoro.

14. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

$R^5$  is trifluoromethyl.

15. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^6$  is hydrogen.

16. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^7$  is hydrogen.

17. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>8</sup> is selected from: hydrogen, C<sub>1</sub>-3alkyl, which is unsubstituted or substituted with 1-6 fluoro, -O-C<sub>1</sub>-3alkyl, fluoro, and hydroxy.

18. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>8</sup> is selected from: hydrogen, methyl, ethyl, trifluoromethyl, fluoro, and -O-CH<sub>3</sub>.

19. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>9</sup> is hydrogen and R<sup>10</sup> is hydrogen.

20. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>8</sup> and R<sup>10</sup> are joined together by a -CH<sub>2</sub>CH<sub>2</sub>- chain or a -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>- chain to form a cyclopentyl ring or a cyclohexyl ring.

21. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>27</sup> is =O, where R<sup>27</sup> is oxygen and is connected via a double bond.

22. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>9</sup> and R<sup>29</sup> are joined together by a C<sub>1</sub>-3alkyl chain to form a ring.

23. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>29</sup> is hydrogen, R<sup>30</sup> is hydrogen, and R<sup>31</sup> is hydrogen.

24. Canceled

25. (currently amended) A pharmaceutical composition which comprises an inert carrier and a the compound of Claim 1, or a pharmaceutically acceptable salt thereof.

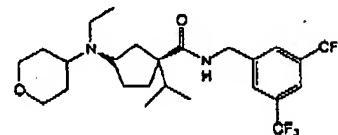
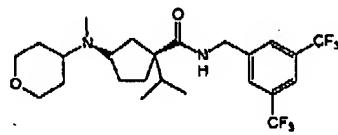
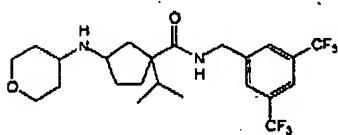
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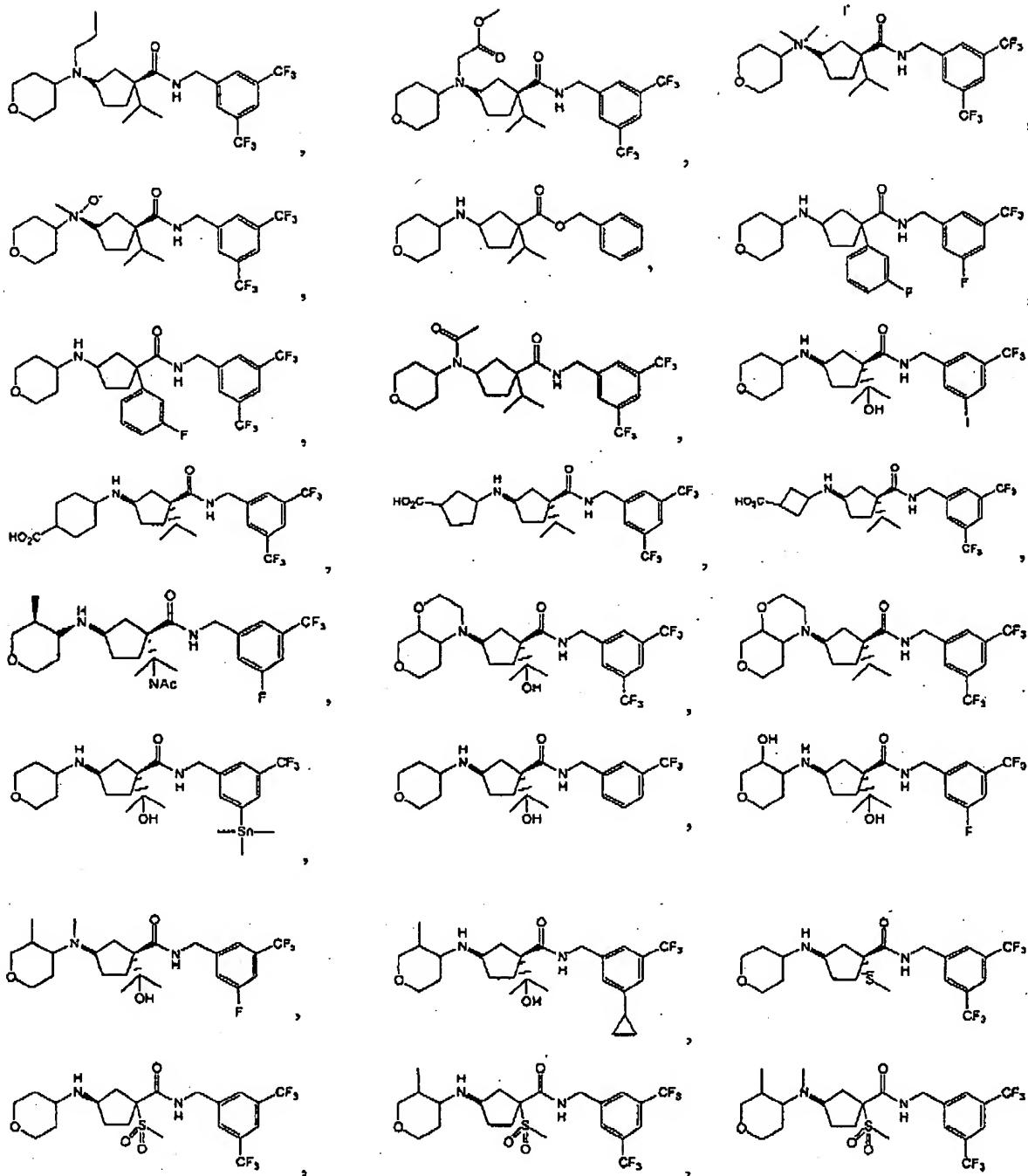
27. (currently amended) A method for treating, ameliorating or controlling an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 4, 1, or a pharmaceutically acceptable salt thereof.

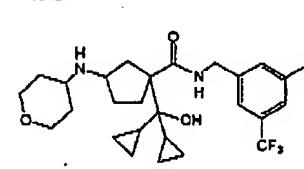
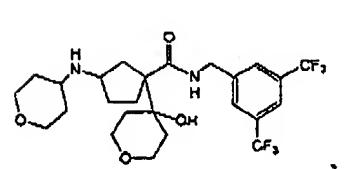
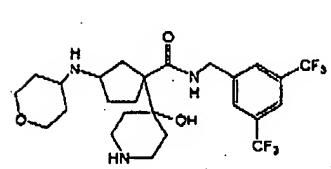
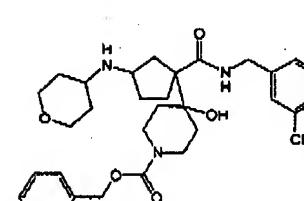
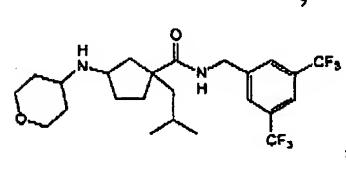
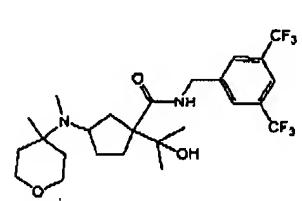
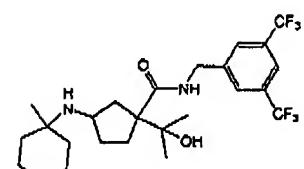
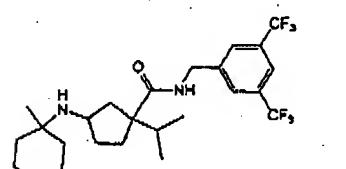
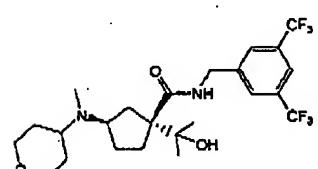
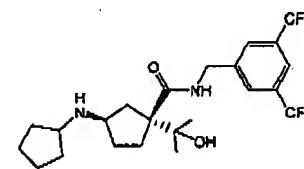
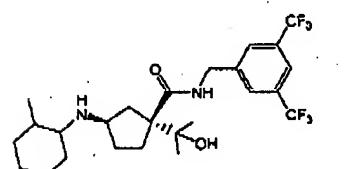
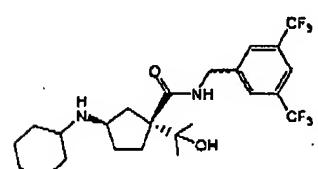
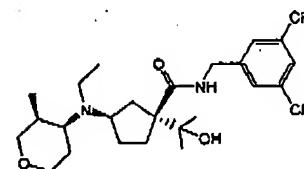
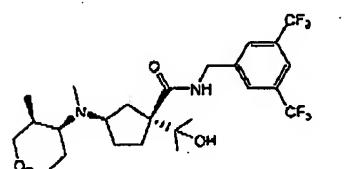
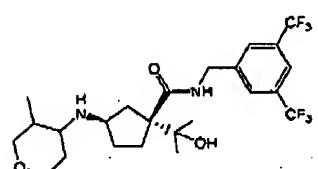
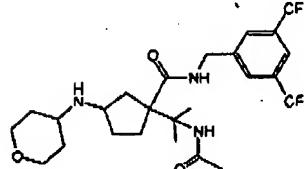
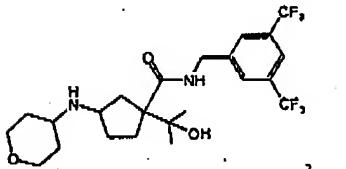
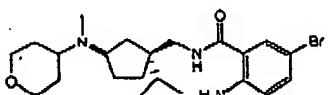
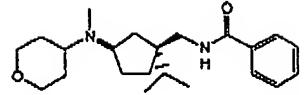
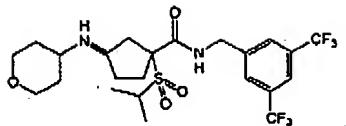
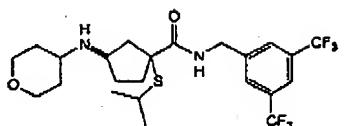
28. (currently amended) A method for reducing the risk of an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 4, 1, or a pharmaceutically acceptable salt thereof.

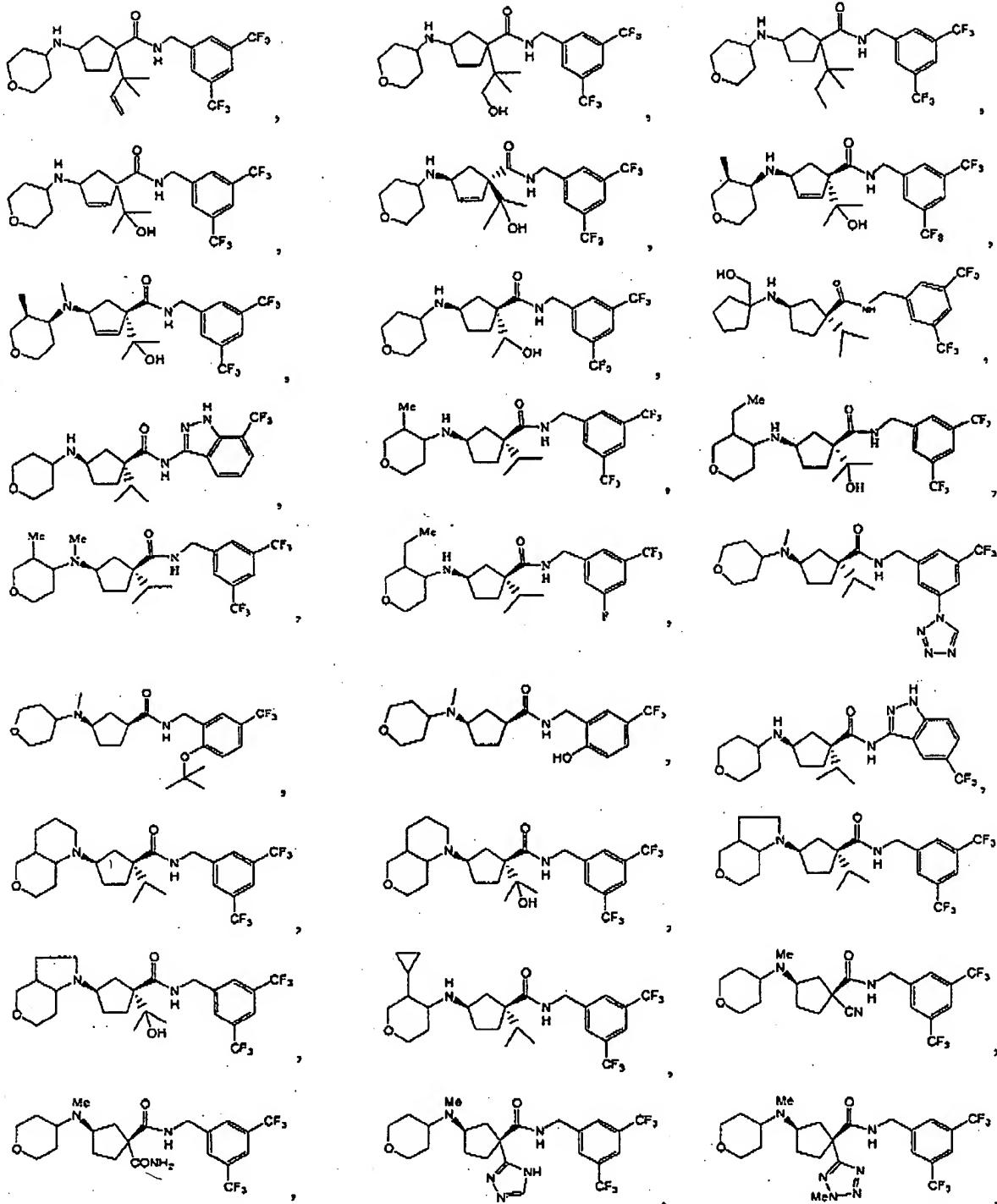
29. (currently amended) A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1, or a pharmaceutically acceptable salt thereof.

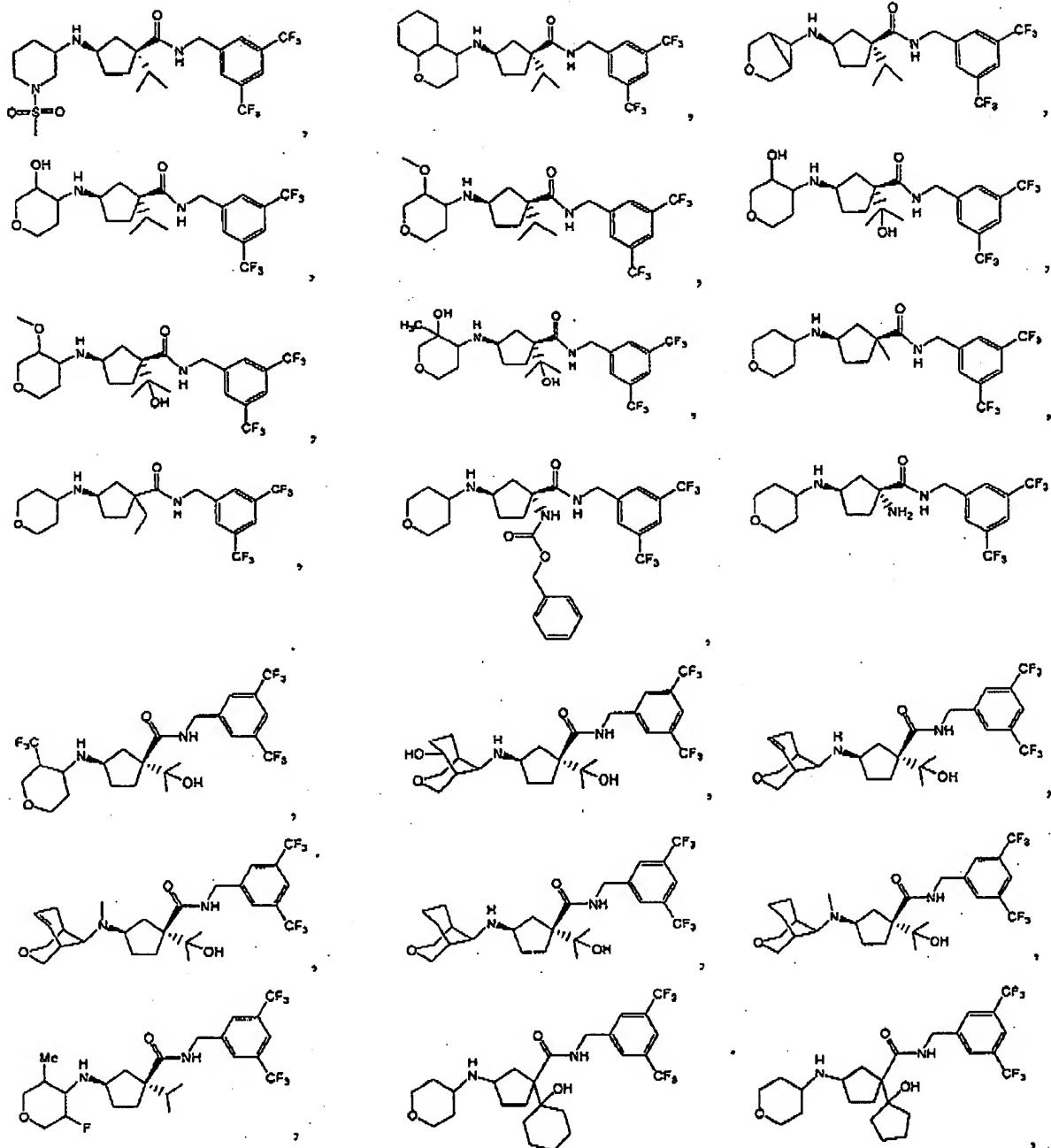
30. (previously presented) A compound which is selected from the group consisting of:



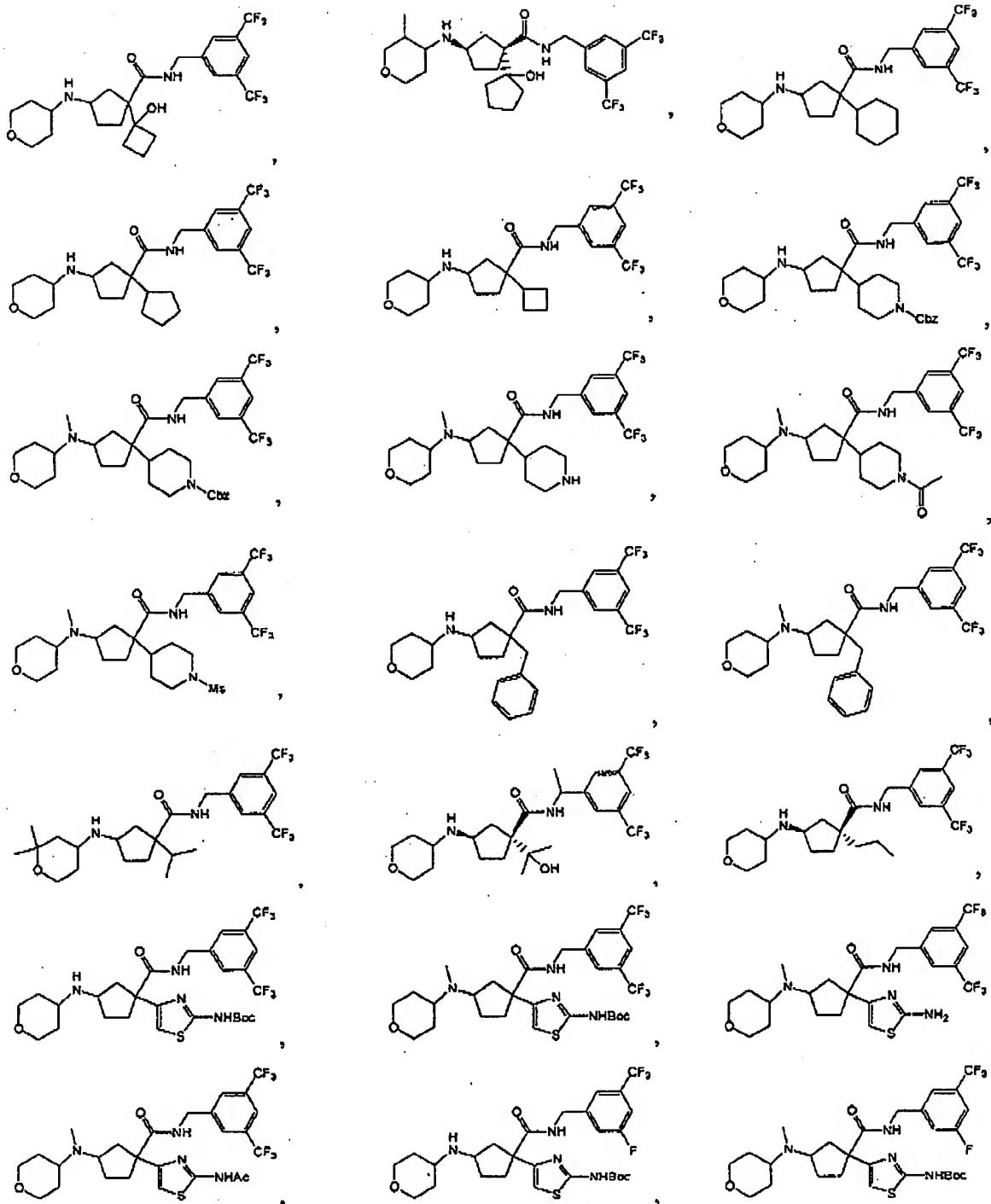
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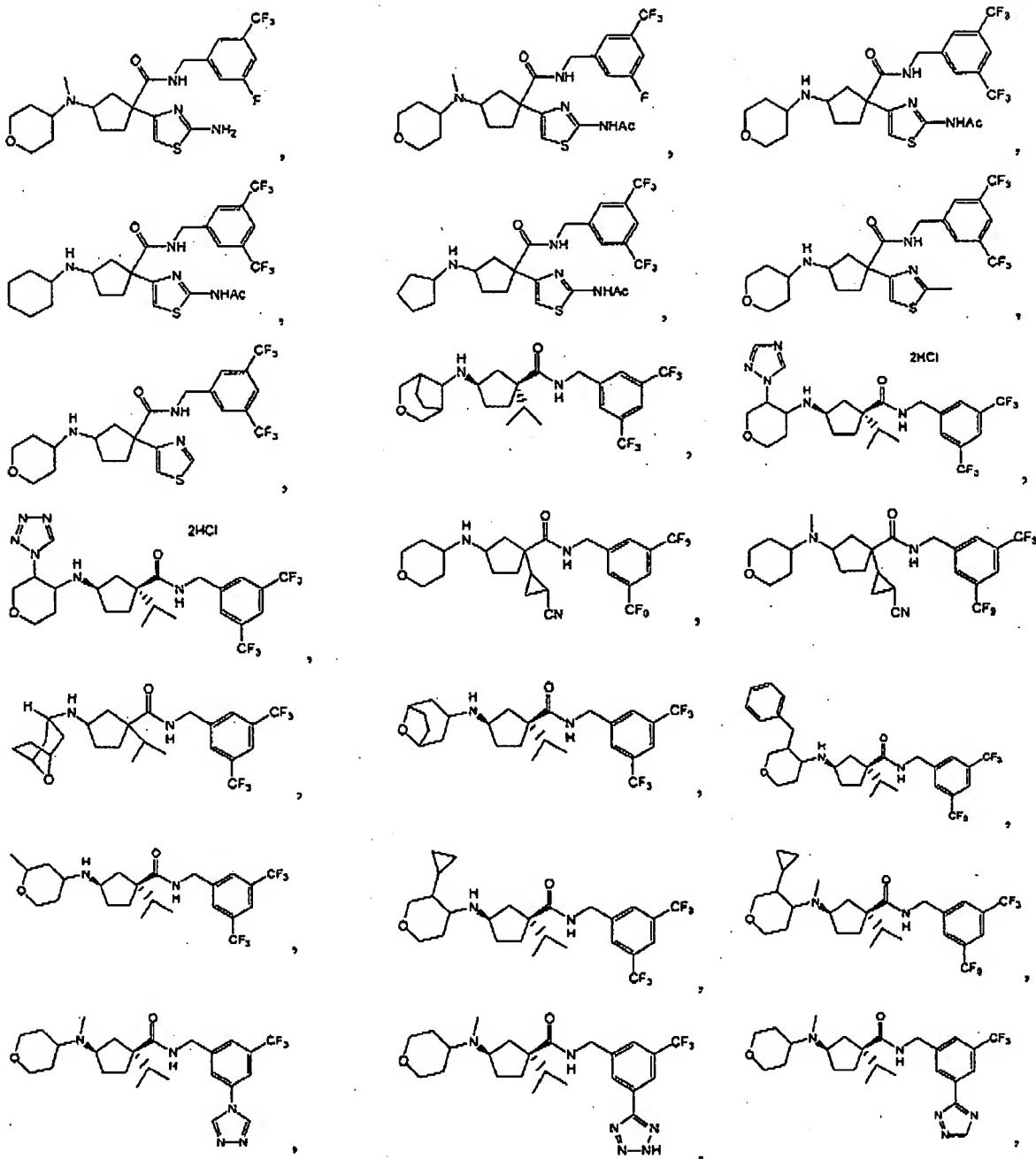
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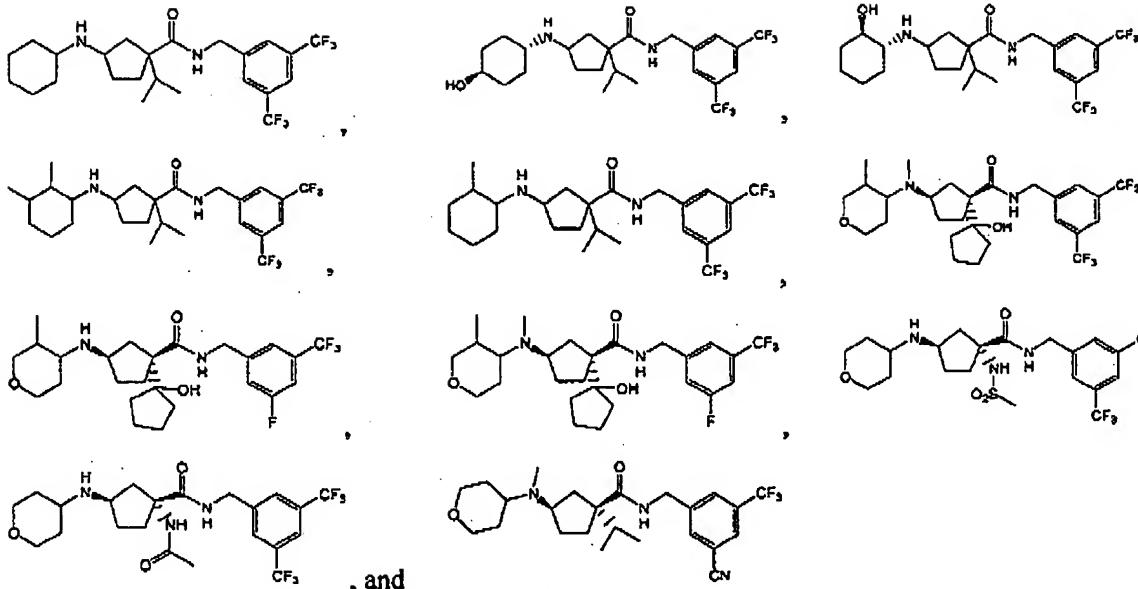
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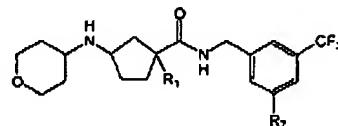
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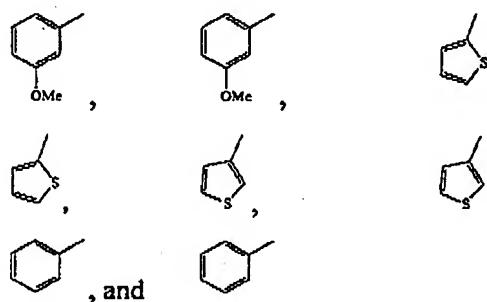
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and pharmaceutically acceptable salts thereof and individual diasteromers thereof.

31. (previously presented) A compound of the formula:

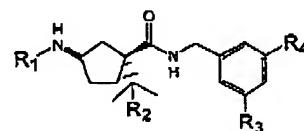


wherin R<sub>7</sub> is F or CF<sub>3</sub>, and wherein R<sub>1</sub> is selected from:

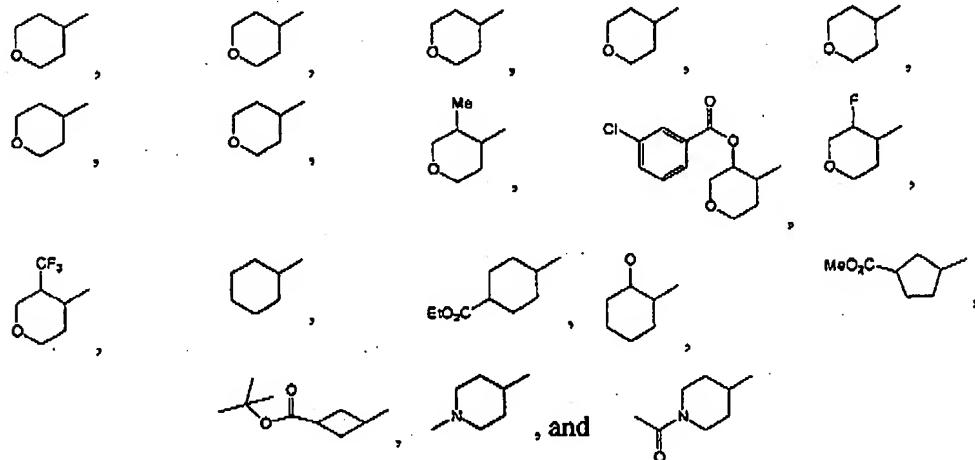


and pharmaceutically acceptable salts thereof and individual diastercomers thereof.

32. (previously presented) A compound of the formula:

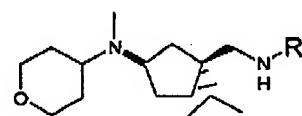


wherein  $\text{R}_2$  is H or OH, wherein  $\text{R}_3$  is F or  $\text{CF}_3$ , wherein  $\text{R}_4$  is  $\text{CF}_3$ , Ph,  $\text{OCF}_3$ , Cl, or  , and wherein  $\text{R}_1$  is selected from:

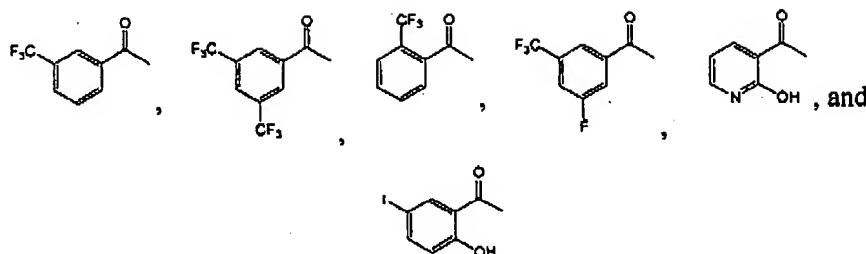


and pharmaceutically acceptable salts thereof and individual diastercomers thereof.

33. (previously presented) A compound of the formula:

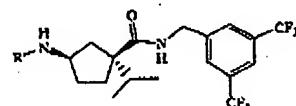


wherein R is selected from:

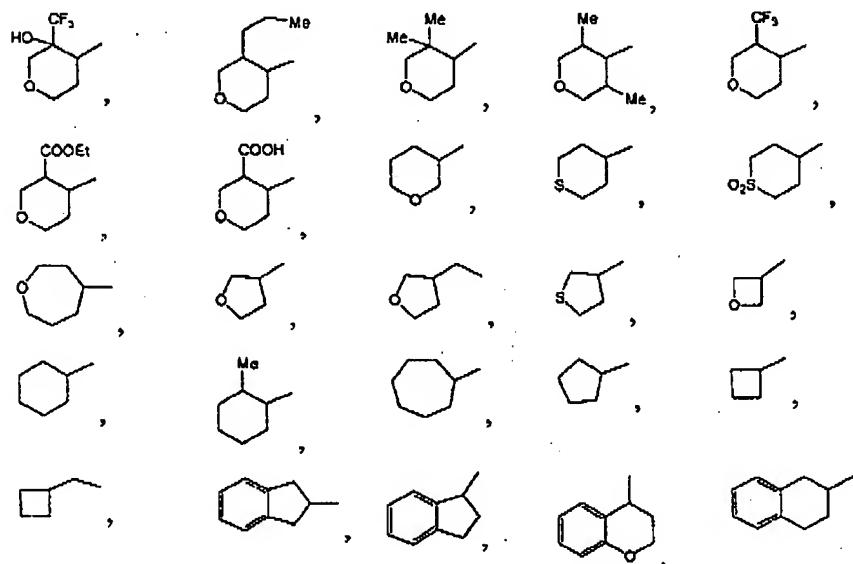


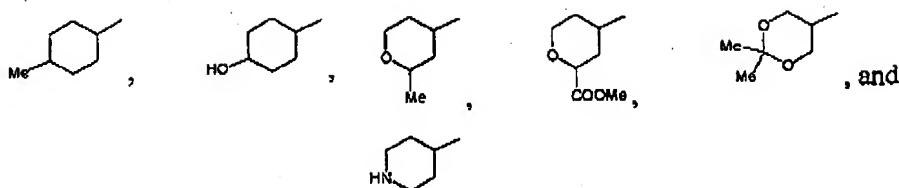
and pharmaceutically acceptable salts thereof and individual diasteromers thereof.

34. (previously presented) A compound of the formula:



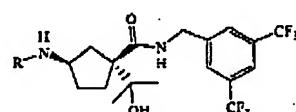
wherein R is selected from:



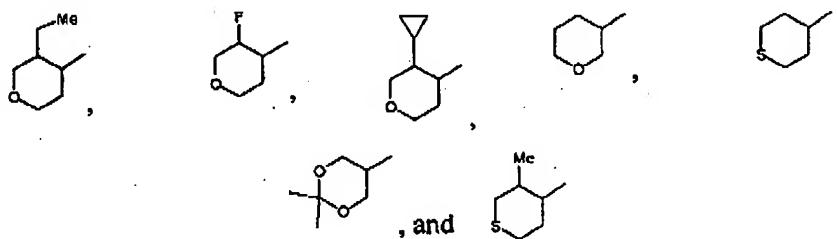
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and pharmaceutically acceptable salts thereof and individual diastercomers thereof.

35. (previously presented) A compound of the formula:

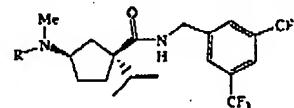


wherein R is selected from:

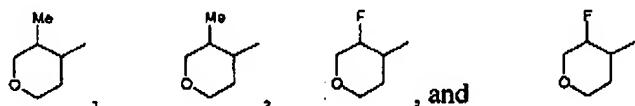


and pharmaceutically acceptable salts thereof and individual diastercomers thereof.

36. (previously presented) A compound of the formula:



wherein R is selected from:



and pharmaceutically acceptable salts thereof and individual diastercomers thereof.